CONCLUSION

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 342312001600. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: February 21, 2001 By: _____

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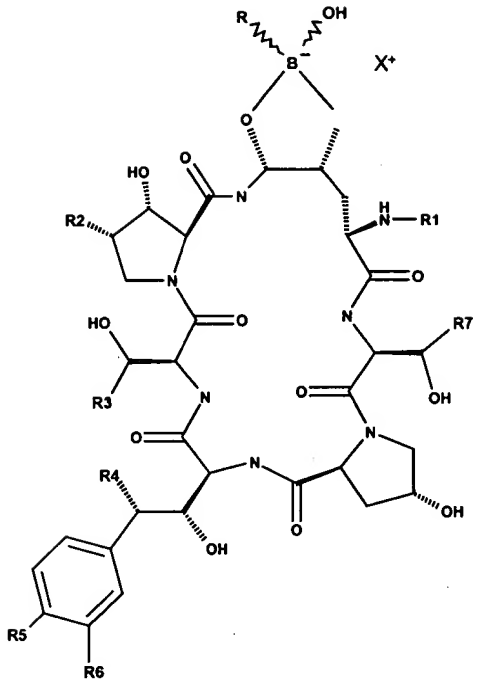
Appendix A

1. A reversible cyclic peptide adduct comprising a boric or boronic acid complexed with a cyclic peptide having at least one 1,2-cis-diol moiety wherein said adduct is more water-soluble than said cyclic peptide having at least one 1,2-cis-diol moiety.

2. The reversible adduct of Claim 1 wherein said boronic acid is selected from the group consisting of alkylboronic acids, heterocycloalkyl boronic acids, arylboronic acids, and heteroarylboronic acids.

3. The reversible adduct of Claim 1 wherein said boronic acid is selected from the group consisting of ethylboronic acid, propylboronic acid, butylboronic acid, tetrahydrofuranylboronic acid, phenylboronic acid, o-methylphenyl-boronic acid, *m*-aminophenylboronic acid, *p*-methylphenyl-boronic acid, *p*-carboxyphenylboronic acid, [*o*-(diisopropylamino)carbonyl] phenylboronic acid, *o*-formylphenylboronic acid, *m*-formylphenylboronic acid, *p*-methoxyphenylboronic acid, *p*-nitrophenylboronic acid, *p*-fluorophenylboronic acid, *p*-bromophenylboronic acid, *p*-trifluoromethylphenylboronic acid, 4,4'-diphenyldiboronic acid, 1-naphthylboronic acid, thiophene-2-boronic acid, thiophene-3-boronic acid, 2-formylthiophene-2-boronic acid, 5-chlorothiophene-2-boronic acid, 5-acetylthiophene-2-boronic acid, benzo[b]thiophene-2-boronic acid, benzo[b]furan-2-boronic acid, indole-5-boronic acid.

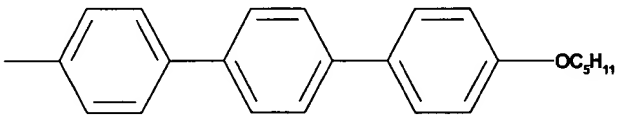
4. The reversible adduct of Claim 1 having the following structure



wherein R is a hydroxy, an alkoxy group, a phenoxy group, an alkyl group, a phenyl group, a thiol, a thioalkyl group, or a thiophenyl group; R^1 is -H or $-C(O)R^{1a}$ where R^{1a} is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, or heteroaryl group; R^2 is -H or $-CH_3$; R^3 is -H, $-CH_3$, $-CH_2CONH_2$ or $-CH_2CH_2NH_2$; R^4 is -H or -OH; R^5 is -OH, $-OPO_3H_2$, or $-OSO_3H$; R^6 is -H or $-OSO_3H$; and X^+ is a cation.

5. The reversible adduct of Claim 4 wherein R is a *m*-aminophenyl group.

6. The reversible adduct of Claim 4 wherein R^{1a} has the following structure



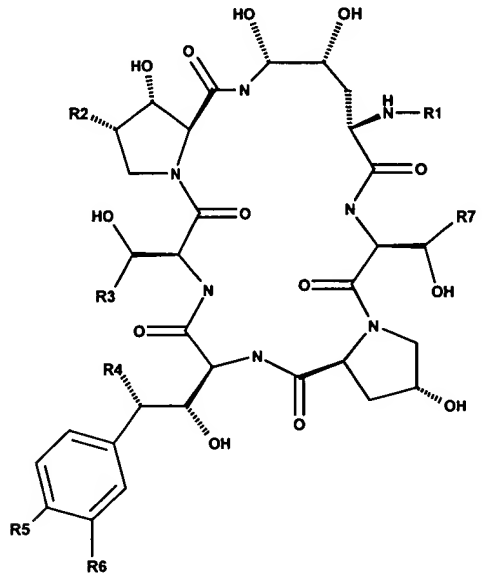
7. A method for forming a reversible cyclic peptide adduct comprising the steps of

(i) providing an aqueous solution of a boric or boronic acid,

(ii) adding a cyclic peptide compound having at least one 1,2-*cis*-diol moiety to said aqueous solution, and

(iii) adjusting the pH of said aqueous solution to a value sufficient to effect complexation between said boric or boronic acid and said cyclic peptide compound.

8. The method of Claim 7 wherein said cyclic peptide has the following structure



wherein R^1 is -H or -C(O)R^{1a} where R^{1a} is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, or heteroaryl group; R^2 is -H or -CH_3; R^3 is -H, -CH_3, -CH_2CONH_2 or -$CH_2CH_2NH_2$; R^4 is -H or -OH; R^5 is -OH, -OPO_3H_2, or -OSO_3H; and R^6 is -H or -OSO_3H.

9. The method of Claim 7 wherein said boronic acid is selected from the group consisting of alkylboronic acids, heterocycloalkyl boronic acids, arylboronic acids, and heteroarylboronic acids.

10. The method of Claim 7 wherein said boronic acid is selected from the group consisting of ethylboronic acid, propylboronic acid, butylboronic acid, tetrahydrofuranylboronic acid, phenylboronic acid, o-methylphenyl-boronic acid, *m*-aminophenylboronic acid, *p*-methylphenyl-boronic acid, *p*-carboxyphenylboronic acid, [*o*-(diisopropylamino)carbonyl] phenylboronic acid, *o*-formylphenylboronic acid, *m*-formylphenylboronic acid, *p*-methoxyphenylboronic acid, *p*-nitrophenylboronic acid, *p*-fluorophenylboronic acid, *p*-bromophenylboronic acid, *p*-trifluoromethylphenylboronic acid, 4,4'-diphenyldiboronic acid, 1-naphthylboronic acid, thiophene-2-boronic acid, thiophene-3-boronic acid, 2-formylthiophene-2-boronic acid, 5-chlorothiophene-2-boronic acid, 5-acetylthiophene-2-boronic acid, benzo[b]thiophene-2-boronic acid, benzo[b]furan-2-boronic acid, indole-5-boronic acid.

11. The method of Claim 7 wherein said aqueous solution is adjusted to a pH value between 7.5 and 9.5.

12. A method for purifying a cyclic peptide having a 1,2-*cis*-diol moiety comprising in the following order the steps of

(i) providing a crude mixture of a cyclic peptide having a least one 1,2-cis-diol functionality,

(ii) complexing said at least one 1,2-cis-diol functionality of said cyclic peptide with a boric or boronic acid to form a reversible adduct,

(iii) solubilizing said reversible adduct in an aqueous solution,

(iv) removing any insoluble materials from said aqueous solution,

(v) acidifying said aqueous solution to a pH value equal to or less than the pKa of said boric or boronic acid, and

(vi) recovering said cyclic peptide from said aqueous solution.

13. A method of purifying a 1,2-*cis*-diol cyclic peptide comprising in the following order the steps of

(a) providing a crude mixture of a cyclic peptide having a least one 1,2-*cis*-diol functionality,

(b) complexing said at least one 1,2-*cis*-diol functionality of said cyclic peptide with a boric or boronic acid to form a reversible adduct,

(c) solubilizing said reversible adduct in an aqueous solution,

(d) concentrating said aqueous solution to form a concentrate,

(e) absorbing said concentrate onto a reverse-phase hydrophobic resin packed in a chromatography column,

(f) eluting with an aqueous solvent system, and

(g) combining effluent fractions containing said reversible adduct into a single effluent solution,

(h) acidifying said effluent solution to a pH value equal to or less than the pKa of said boric or boronic acid to decomplex said reversible adduct, and

(i) recovering said cyclic peptide from said acidified effluent solution.

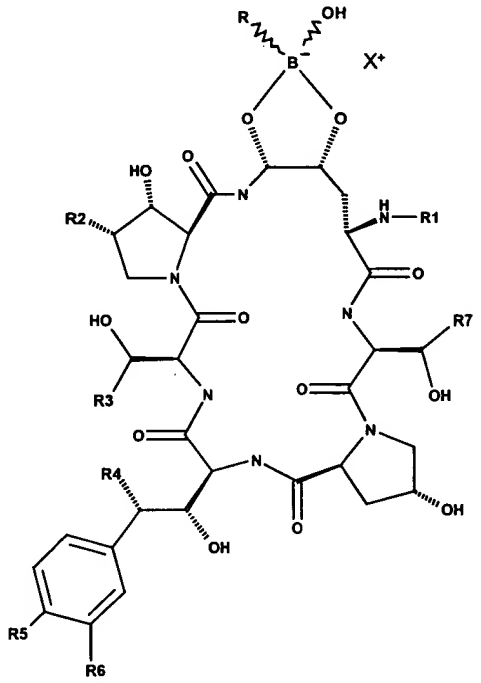
14. A pharmaceutical formulation comprising a reversible adduct comprising a complex of a boric or boronic acid with a cyclic peptide having a 1,2-*cis*-diol moiety.

15. The pharmaceutical formulation of Claim 14 further comprising a pharmaceutically inert carrier.

16. The pharmaceutical formulation of Claim 15 wherein said inert carrier is water.

17. The pharmaceutical composition of Claim 14 further comprising a wetting agent, lubricating agent, emulsifier, suspending agent, preservative, sweetener, stabilizer, perfuming agent, flavoring agent or combinations thereof.

18. The pharmaceutical formulation of Claim 14 wherein said reversible adduct has the following structure



wherein R is a hydroxy, an alkoxy group, a phenoxy group, an alkyl group, a phenyl group, a thiol, a thioalkyl group, or a thiophenyl group; R^1 is -H or $-C(O)R^{1a}$ where R^{1a} is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, or heteroaryl group; R^2 is -H or $-CH_3$; R^3 is -H, $-CH_3$, $-CH_2CONH_2$ or $-CH_2CH_2NH_2$; R^4 is -H or -OH; R^5 is -OH, $-OPO_3H_2$, or $-OSO_3H$; R^6 is -H or $-OSO_3H$; X^+ is a cation; and pharmaceutically acceptable hydrates, esters and salts thereof.

19. The pharmaceutical formulation of Claim 18 wherein R is a *m*-aminophenyl group.

20. A method for treating a fungal infection comprising in the following order the steps of

(a) providing a host in need of treatment for a fungal infection,

(b) administrating an effective dose of a reversible adduct according to Claim 4, and

(c) decomplexing said reversible adduct to release a pharmaceutically active 1,2-*cis*-diol, cyclic peptide.

21. The method of Claim 20 wherein said reversible adduct is administered by means of an aqueous solution.

22. The method of Claim 20 wherein said reversible adduct is administered by means of an aqueous IV solution.